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PATENT COOPERATION TREATY

DEF

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

GATES, Edward R.
WOLF, GREENFIELD & SACKS,
600 Atlantic Avenue
Boston, MA 02210
ETATS-UNIS D'AMERIQUE

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WRITTEN OPINION

(PCT Rule 66)

Date of mailing
(day/month/year)

18/03/2002

Applicant's or agent's file reference

E0355/7003WO

REPLY DUE

within 2 / 00 months/days
from the above date of mailing

International application No.

PCT/US 00/ 28747

International filing date (day/month/year)

18/10/2000

Priority date (day/month/year)

18/10/1999

International Patent Classification (IPC) or both national classification and IPC

C12N15/63

Applicant

EMORY UNIVERSITY

1. This written opinion is the first drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is:

18/02/2002

Name and mailing address of the IPEA/

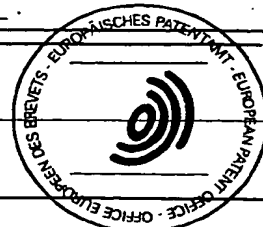


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Authorized officer

Examiner

Formalities officer
(incl. extension of time limits)
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I. Basis of the opinion

The basis of this written opinion is the application as originally filed.

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question of whether the claimed invention appears to be novel, to involve an inventive step, or to be industrially applicable has not been and will not be the subject of the international preliminary examination in respect of the claims which have not been searched (Article 17(2)(a) or (3) and Rule 66.1(e) PCT; see also international search report).

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability

1. To the extent that the international preliminary examination has been carried out (see item III above), the following is pointed out:
2. In light of the documents cited in the international search report, it is considered that the invention as defined in at least some of the claims, which have been the subject of an international search report, does not appear to meet the criteria mentioned in Article 33(1) PCT, i.e. does not appear to be novel and/or to involve an inventive step (see international search report, in particular the documents cited X and/or Y and corresponding claim references).
3. If amendments are filed, the applicant should comply with the requirements of Rule 66.8 PCT and indicate the basis of the amendments in the documents of the application as originally filed (Article 34 (2) (b) PCT) otherwise these amendments may not be taken into consideration for the establishment of the international preliminary examination report. The attention of the applicant is drawn to the fact that if the application contains an unnecessary plurality of independent claims, no examination of any of the claims will be carried out.

PATENT COOPERATION TREATY

Subject to STA? YES/NO

per docket/ECB

Gm 7-8-02

1AD

From the

INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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To:

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Boston, MA 02210
ETATS-UNIS D'AMERIQUE

DOCKETED

JUL 11 2002

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year)

04.07.2002

Applicant's or agent's file reference
E0355/7003WO

IMPORTANT NOTIFICATION

International application No.
PCT/US00/28747

International filing date (day/month/year)
18/10/2000

Priority date (day/month/year)
18/10/1999

Applicant
EMORY UNIVERSITY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

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Tel. +49 89 2399 - 0 Tx: 523656 epmu d
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Authorized officer

Zoglauer, H

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference E0355/7003WO		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/28747	International filing date (day/month/year) 18/10/2000	Priority date (day/month/year) 18/10/1999	
International Patent Classification (IPC) or national classification and IPC C12N15/63			
Applicant EMORY UNIVERSITY			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 			
Date of submission of the demand 09/05/2001		Date of completion of this report 04.07.2002	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Roscoe, R Telephone No. +49 89 2399 2554	



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/28747

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-80 as originally filed

Claims, No.:

1-109 as originally filed

Drawings, sheets:

1/17-17/17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/28747

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☒ the entire international application.

☐ claims Nos. .

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/28747

The documents mentioned in the present written opinion / International Preliminary Examination Report are numbered as in the search report, i.e. D1 corresponds to the first document of the search report etc.

III. No Opinion

No opinion is expressed for the set of claims as a whole since it comprises an excessive number of claims, in particular independent claims (about 23), many of which cover essentially the same or very significantly overlapping subject-matter. Nevertheless, for the benefit of the applicant an opinion is given below with respect to the subject-matter of the application in broad terms.

General Comments on Claimed subject-matter with respect to cited prior art:

Although documents D1, D5 and D6 refer to TMS-1 methylation in the context of cancers, none of these documents actually enable a skilled person to use this knowledge. TMS-1 was not technically defined in any of these documents and the first deposited Genbank sequences showing TMS-1 and identifying it as such were only available after the priority date of the present application (i.e. matter not entitled to priority would be unlikely to be considered inventive in view of these documents, since they disclose the underlying principle of the invention).

D1 is highly relevant to claims 95-99 of the present application since these relate to a vague method of identifying genes which are transcriptionally downregulated following methylation which is disclosed in D1. Details missing in D1 are merely trivial.

D3 discloses the TMS-1 gene without naming it in this way. The gene was identified as being overexpressed in human breast tumors (p.89). No mention of regulation by methylation was made. In contrast, the gene is considered to be underexpressed due to methylation-induced silencing by applicant. This difference could well be a basis for medical claims to particular applications of TMS-1. The D3 sequences show 100% identity to TMS-1 (DNA - Seq.ID No.21, Protein - Seq.ID No.84) in the reading frame of the gene. Related matter such as vectors, host cells etc. are of course also disclosed. This essentially means that

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/28747

applicant will not be entitled to claim TMS-1 DNA or proteins or related products.

D4 is not relevant in the Intl. Phase, but would be relevant prior art upon entry into a European Regional Phase. D4 discloses TMS-1 under the name hCARD5 and suggests that it, or specifically its CARD domain could be used to treat cancer.

It is noted that treating a disorder characterized by abnormal methylation using TMS-1 or derivatives may not be novel or inventive (since many disorders intrinsically have this property), yet claims involving treatment by demethylation or diagnosis by assessing methylation levels, for example may possibly be considered novel & inventive.